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Paper 8
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AQUESTIVE THERAPEUTICS, INC.,
Petitioner,

v.

NEURELIS, INC.,
Patent Owner.

Case IPR2019-00450
Patent 9,763,876 B2

Before ZHENYU YANG, JON B. TORNQUIST, and JAMIE T. WISZ, *Administrative Patent Judges.*

TORNQUIST, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. §§ 314, 325(d)

I. INTRODUCTION

Aquestive Therapeutics, Inc. ("Petitioner") filed a Petition (Paper 2, "Pet.") requesting an *inter partes* review of claims 1–36 of U.S. Patent No. 9,763,876 B2 (Ex. 1001, "the '876 patent"). Neurelis, Inc.[1] ("Patent Owner") filed a Preliminary Response to the Petition (Paper 6, "Prelim. Resp.").

For the reasons explained below, we exercise our discretion under 35 U.S.C. §325(d) and decline to institute an *inter partes* review on the grounds set forth in the Petition.

A. Related Proceedings

The parties indicate that Petitioner has filed additional petitions against the '876 patent in IPR2019-00449 and IPR2019-00451. Pet. 2; Paper 7, 2.

B. The '876 Patent

The '876 patent is directed to nasally administered pharmaceutical solutions containing one or more benzodiazepine drugs. Ex. 1001, 9:14–17. The '876 patent explains that solubility challenges associated with benzodiazepine drugs previously hindered the development of formulations intended for oral, rectal, or parenteral administration. *Id.* at 1:53–57, 19:12–15. It was discovered, however, that vitamin E (which includes tocopherols and tocotrienols) is an effective carrier for benzodiazepine drugs, as these compounds are soluble, or at least partially soluble, in vitamin E. *Id.* at

[1] Patent Owner informs us that subsequent to the filing of the Petition, Hale Biopharma Ventures, LLC, the originally named Patent Owner in this case, assigned its rights in the '876 patent to Neurelis, Inc. Paper 7, 2 (citing Reel 048271; Frame 0304).

33:8–13, 33:42–45. The ’876 patent also reports that vitamin E “can have the added benefit of either avoiding irritation of sensitive mucosal membranes and/or soothing irritated mucosal membranes.” *Id.* at 33:47–49.

The ’876 patent discloses that one or more lower alcohols, such as ethanol and benzyl alcohol, may be used in the formulation. *Id.* at 2:57–64, 33:55–67 (noting that to “avoid the drawbacks of emulsions,” the disclosed solutions contain vitamin E and “one or more lower alkyl alcohols”). In addition, an alkyl glycoside may be added to the formulation to act as a penetration enhancer. *Id.* at 34:2–9.

C. Illustrative Claim

Petitioner challenges claims 1–36 of the ’876 patent. Independent claim 1 is illustrative of the challenged claims and is reproduced below:

> 1. A method of treating a patient with a disorder which is treatable with a benzodiazepine drug, comprising: administering to one or more nasal mucosal membranes of a patient a pharmaceutical solution for nasal administration consisting of a benzodiazepine drug, one or more natural or synthetic tocopherols or tocotrienols, or any combinations thereof, in an amount from about 30% to about 95% (w/w); ethanol and benzyl alcohol in a combined amount from about 10% to about 70% (w/w); and an alkyl glycoside.

Ex. 1001, 63:26–34.

D. The Asserted Ground of Unpatentability

Petitioner contends the subject matter of claims 1–36 of the ’876 patent would have been obvious in view of the combined disclosures of Sonne[2] and Meezan.[3] Pet. 5–6. In support of its obviousness arguments,

[2] US 6,193,985 B1, issued February 27, 2001 (Ex. 1013).

[3] US Pub. No. 2006/0046962 A1, published March 2, 2006 (Ex. 1011).

Petitioner relies on the declaration testimony of Dr. Nicholas A. Peppas. Ex. 1041; Pet. 5.

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, claim terms are construed using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. § 282(b). 37 C.F.R. § 42.100(b). Under this claim construction standard, claim terms are given their ordinary and customary meaning as would be understood by one of ordinary skill in the art at the time of the invention. *See id.*; *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). A patentee may define a claim term in a manner that differs from its ordinary and customary meaning; however, any special definitions must be set forth in the specification with reasonable clarity, deliberateness, and precision. *See In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner provides proposed constructions for the terms "vitamin E," "bioavailability," "% (w/w)," "% (w/v)," and "about 56.47% (w/v) vitamin E." Pet. 13–17. Patent Owner contends Petitioner's constructions for "vitamin E," "bioavailability," "% (w/w)," and "% (w/v)" are consistent with the use of those terms in the specification and claims of the '876 patent, but finds fault with the reasoning and support provided by Petitioner for its construction of the term "about 56.47% (w/v) vitamin E." Prelim. Resp. 3–5.

Upon review of the parties' arguments and supporting evidence, we determine that no claim terms require construction for purposes of this Decision. *See Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*,

868 F.3d 1013, 1017 (Fed. Cir. 2017) (citing *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("[O]nly those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy.")).

B. 35 U.S.C. § 325(d)

Institution of *inter partes* review is discretionary. *See Harmonic Inc. v. Avid Tech, Inc.*, 815 F.3d 1356, 1367 (Fed. Cir. 2016). Pursuant to 35 U.S.C. § 325(d), the Board may take into account whether, and reject the petition because, "the same or substantially the same prior art or arguments previously were presented to the Office."

In evaluating whether to exercise our discretion under § 325(d), we consider several non-exhaustive factors, including:

> (a) the similarities and material differences between the asserted art and the prior art involved during examination;
>
> (b) the cumulative nature of the asserted art and the prior art evaluated during examination;
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> (c) the extent to which the asserted art was evaluated during examination, including whether the prior art was the basis for rejection;
>
> (d) the extent of the overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art;
>
> (e) whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the asserted prior art; and
>
> (f) the extent to which additional evidence and facts presented in the Petition warrant reconsideration of the prior art or arguments.

Becton, Dickinson and Co. v. B. Braun Melsungen AG, IPR2017-01586, slip op. at 17–18 (Paper 8) (PTAB Dec. 15, 2017) (informative). We refer to these non-exhaustive factors as the "*Becton Dickinson* factors."

Patent Owner requests that we deny institution of *inter partes* review under § 325(d) because Sonne and Meezan were examined in depth by the Examiner during prosecution, and all of the *Becton Dickinson* factors weigh in favor of denying institution. Prelim. Resp. 5–24.

Anticipating Patent Owner's arguments, Petitioner asserts § 325(d) should not bar institution in this case because (1) the Examiner failed to fully consider Sonne's teachings; (2) the Examiner was misled by the Applicants' faulty interpretation of Sonne's disclosures; (3) the Petition presents the Sonne and Meezan references "in a new light"; and (4) Petitioner's arguments are accompanied by the declaration testimony of Dr. Peppas, which was not before the Examiner during prosecution of the involved patent family.[4] Pet. 6–11.

Upon review of the relevant prosecution history and the arguments made in the Petition, we find that the *Becton Dickinson* factors weigh in favor of exercising our discretion under 35 U.S.C. § 325(d) to deny institution of an *inter partes* review.

1. Factors (a) and (c)

Becton Dickinson factor (a) looks to whether the same prior art or arguments were previously presented to the Office. Factor (c) looks to

[4] Petitioner also argues that the Petition applies a different legal theory than discussed during prosecution. Pet. 11. It is not clear what legal theory Petitioner is referring to, however, as both the Petition and the Examiner address obviousness under 35 U.S.C. §103(a). Pet. 5; Ex. 1004, 2124.

whether this art was evaluated during examination, including whether it was the basis for a rejection. To fully evaluate factors (a) and (c), as well as factors (b), (d), (e), and (f) discussed below, we provide a detailed review of the prosecution history of record for the '876 patent family.

a. The '876 Patent Family

The '876 patent was filed as U.S. Application No. 14/527,613 ("the '613 application"), and is a continuation of U.S. Application No. 13/495,942 ("the '942 application") (issued as U.S. Patent No. 8,895,546 ("the '546 patent"), which is in turn a continuation-in-part ("CIP") of U.S. Application No. 12/413,439 ("the '439 application"). Ex. 1001, (63).

Each of the identified patent applications was examined by the same patent Examiner. *See* Ex. 1002, 165; Ex. 1004, 2034; Ex. 1007, 447 (identifying the Examiner for each application as Adam C. Milligan).[5]

b. Prosecution History of the '439 Application

The '439 application was filed on March 27, 2009. Ex. 1007, 86; Ex. 1001, (63). Pursuant to a restriction requirement, the Applicants elected to prosecute original claims 20–47, with independent claim 20 directed to a method of treating a patient with a benzodiazepine drug comprising:

administering to one or more nasal mucosal membranes of a patient (1) a benzodiazepine drug, (2) one or more natural or synthetic tocopherols or tocotrienols, or any combination thereof, in an amount from about 30% to about 95% (w/w), and (3) one or more alcohols or glycols, or any

[5] Our citations to the prosecution histories in Exhibits 1002, 1004, and 1007 are to the pages numbers added in the lower right corner of the Exhibits.

combinations thereof, in an amount from about 10% to about 70% (w/w). Ex. 1007, 459, 464.

In a March 18, 2011 Office Action, the Examiner rejected pending claims 20–24 and 27–45 in view of Sonne, reasoning that Sonne discloses compositions containing a benzodiazepine drug in an amount of 0.0001% to 40%, tocopherol in an amount from 20 to 99.9%, and the use of one or more co-solvents, such as ethanol and benzyl alcohol, to optimize bioadhesion, sprayability, and viscosity of the formulation. *Id.* at 477–478 (citing Ex. 1013, 1:7–14, 5:56–61, 6:47–53, 8:28–43 (noting that ethanol may be used in an amount of about 11% by weight of the formulation), 11:1–13 (Example 11)).[6] The Examiner also rejected pending claims 25, 26, 46, and 47 in view of the combined disclosures of Sonne and Meezan, noting that Meezan discloses the use of nanoparticles (claims 25 and 26) and the use of an alkyl glycoside (claims 46 and 47) to improve drug absorption. *Id.* at 480–481.

Despite the fact that each individual limitation of claim 1 was expressly disclosed in Sonne, the Examiner found that Sonne required "too much 'picking and choosing' to give rise to anticipation." *Id.* at 478. The Examiner determined, however, that one of ordinary skill in the art would have found it obvious to select "the various combinations of features claimed from within the prior art disclosure (specifically, diazepam, alcohol or glycol, and α-tocopherol) to arrive at the instantly claimed subject matter." *Id.*

[6] The Examiner and Applicants did not cite to "Exhibit 1013" when discussing Sonne. We do so to aid in identification of the Applicants' and Examiner's arguments.

In a September 19, 2011 Response, the Applicants amended pending independent claim 20 to require a pharmaceutical "solution" "consisting of" the identified ingredients. *Id.* at 492. The Applicants argued these added limitations distinguished the pending claims from the prior art because Examples 1–3, 7–11, 17, 19, and 22–23 of Sonne "each describe an oil-in-water emulsion of the benzodiazepine," which is not a "solution" and would fall outside the scope of the claim due to the use of the transitional phrase "consisting of." *Id.* at 501. The Applicants also argued that Sonne discloses that nasal administration of active drugs requires the use of "a high concentration of the oil (or lipid) phase" and "that addition of co-solvents such as ethanol is less desired, since such solutions 'tend to be irritating to certain mucosal tissues.'" *Id.* at 500–502 (citing Ex. 1013, 3:1–4, 3:65–67, 4:14–16) (asserting that "Examples 1–3, 7–11, 17, 19, and 22–23 each describe an oil-in-water emulsion of a benzodiazepine for nasal administration").

The Examiner subsequently issued a final rejection of the claims on November 21, 2011, disagreeing with the Applicants "teaching away" arguments and concluding that "one of ordinary skill in the art would have found it obvious to nasally administer a benzodiazepine composition that contains only tocopherol or tocotrienol, an alcohol and optionally one or more alkyl glycosides." *Id.* at 514–515. The Examiner explained that Sonne must be interpreted broadly and "relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including nonpreferred embodiments." *Id*. at 514. As examples of the broad teachings of Sonne, the Examiner identified its disclosures that: (1) the "compositions of the invention may be used directly as [a] solution of bioactive agents in

the tocopherol solvent" (*id.* at 515 (citing Ex. 1013, 3:60–61)); (2) "[v]iscosity can be reduced by the addition of co-solvents such as ethanol" (*id.* (citing Ex. 1013, 3:65–66)); (3) transmucosal delivery is preferred and nasal administration particularly preferred (*id.* (citing Ex. 1013, 3:54, 3:58–59)); (4) compositions of the invention may contain from 1–99.99% tocopherol (*id.* (citing Ex. 1013, 5:55–57)); (5) co-solvents such as ethanol can be used to optimize the bioadhesion, sprayability, and viscosity of the formulation (*id.* (citing Ex. 1013, 6:47–53)); and (6) ethanol may be present in an amount of about 11% by weight of the formulation (*id.* (citing Ex. 1013, 8:28–43 (Example 3))).

On May 21, 2012, the Applicants filed a Request for Continued Examination ("RCE"), again asserting that Sonne discourages the use of ethanol in nasal sprays due to its irritating nature. *Id.* at 564. The Applicants also reiterated that "Examples 1–3, 7–11, 17, 19, and 22–23 [of Sonne] each describe an oil-in-water emulsion of the benzodiazepine." *Id.*

On June 19, 2014, the Examiner rejected all pending claims, this time with respect to Sonne, Meezan, and Lehat (which was relied on to address the Applicants added claim limitations requiring treatment of a seizure disorder). *Id.* at 2806. In so doing, the Examiner again relied on Sonne's broad disclosures, including its disclosure of using ethanol as a co-solvent to optimize the bioadhesion, sprayability, and viscosity of the nasal spray. *Id.* at 2807 (citing Ex. 1013, 6:47–53).

In a November 19, 2014 Response, the Applicants again argued that Examples 1–3, 7–11, 17, 19, and 22–23 of Sonne describe oil-in-water emulsions containing a benzodiazepine drug, and concluded that because

each of the benzodiazepine compositions taught by Sonne contains oil, one of ordinary skill in the art would not seek to modify the teachings of Sonne to practice the claimed methods. *Id.* at 2832–2833.

In a March 30, 2016 Response,[7] the Applicants correctly noted for the first time that Examples 11 and 16 of Sonne are solutions, not emulsions, but argued that these solutions do not contain alcohol. *Id.* at 3085. Applicants also argued that in no case does Sonne teach or suggest administering an ethanol-containing solution to the nose, and in fact expressly teaches away from using such a solution for nasal applications. *Id.*

In subsequent Office Actions of July 14, 2016, March 30, 2017, and October 19, 2017, the Examiner maintained his position that Sonne's broad disclosures would have led one of ordinary skill in the art to the claimed formulations. *Id.* at 3093–3101, 3309–3320, 3470–3479. Likewise, in subsequent responses, Applicants maintained their position that Sonne, Meezan, and Lehat did not render the pending claims obvious. *Id.* at 3113–3121, 3323–3335. On June 1, 2018, a Notice of Abandonment was issued for the '439 application for failure to reply to the Office Action of October 19, 2017. *Id.* at 3488.

c. Prosecution History of the '942 Application

On June 13, 2012, the Applicants filed the '942 application, which is a CIP of the '439 application and also claims priority to Provisional Application Nos. 61/497,017 and 61/570,110. Ex. 1004, 3; Ex. 1001,

[7] In an Office Action of March 13, 2015, a Response of September 11, 2015, and an Office Action of October 5, 2015, the Applicants and the Examiner addressed the implications of the term "consisting of" with respect to Sonne's disclosures. Ex. 1007, 2939, 2958–59, 2965, 3070–3071.

(60), (63). Pursuant to a preliminary amendment, independent claim 1 of the '942 application recited a pharmaceutical solution for nasal administration consisting of (a) a benzodiazepine drug; (b) one or more tocopherols or tocotrienols, or any combination thereof, in an amount from about 30% to about 95% (w/w); (c) one or more alcohols or glycols, or any combinations thereof, in an amount from about 10% to about 70% (w/w); and (d) an alkyl glycoside. Ex. 1004, 103.

In an Office Action of October 1, 2013, the Examiner rejected all pending claims as having been obvious over the combined disclosures of Sonne and Meezan. *Id.* at 2122, 2125. In this rejection, the Examiner identified the same broad disclosures of Sonne discussed at length during prosecution of the parent '439 application. *Id.* at 2125–2126.

In an April 1, 2014 Response, the Applicants amended the claims to replace "one or more alcohols or glycols, or any combinations thereof" with "ethanol and benzyl alcohol in a combined" amount of from about 10% to about 70% (w/w). *Id.* at 2138–2139. In support of the patentability of these amended claims, the Applicants argued that "[n]either Sonne nor Meezan teaches or suggests using both ethanol and benzyl alcohol" in the claimed amounts and, although Sonne discloses using ethanol as a viscosity-reducing agent, this "teaching appears in the context of introducing the purported benefits of the therein-described colloidal formulations." *Id.* at 2149 (citing Ex. 1013, 3:60–67, 4:1–2). Applicants also argued that Sonne's admonition that solutions containing ethanol can be irritating would have counseled one of ordinary skill in the art to not use higher concentrations of ethanol than are actually used in the Sonne reference. *Id.*

On July 24, 2014, the Examiner issued a Notice of Allowance for all pending claims of the ’942 application. *Id.* at 2560–2565; *see also id.* at 2583–2584 (issuing a Corrected Notice of Allowance).

d. Prosecution History of the ’613 application

The ’613 application is a continuation of the ’942 application. Ex. 1001, (63). Pursuant to a preliminary amendment, the Applicants chose to pursue claims in this application that were drawn to a method of treating a patient with a pharmaceutical solution consisting of (a) a benzodiazepine drug; (b) one or more tocopherols or tocotrienols, or any combinations thereof, in an amount from about 30% to 95% (w/w); (c) ethanol and benzyl alcohol in a combined amount from about 10% to about 70% (w/w); and (d) an alkyl glycoside. Ex. 1002, 148.

In an Office Action of July 14, 2016, the Examiner rejected the pending claims in view of several paragraphs of 35 U.S.C. § 112, and as being unpatentable on the grounds of nonstatutory double patenting over claims of the ’546 patent and the ’439 application. *Id.* at 167–170. The Examiner did not reject any of the pending claims under 35 U.S.C. § 103.

In a January 10, 2017 Response, the Applicants amended several dependent claims to address the Examiner’s § 112 rejections, and indicated they would consider filing a terminal disclaimer should the claims of the ’613 application be found otherwise allowable. *Id.* at 186–193.

The Examiner then issued a final rejection of all pending claims on the grounds of non-statutory double patenting (*id.* at 438–439), the Applicants filed terminal disclaimers with respect to the ’546 patent, the

’439 application, and U.S. Application No. 15/470,498 (*id.* at 478), and the Examiner issued a Notice of Allowance (*id.* at 491–496, 522–524).

e. Conclusion with Respect to Factors (a) and (c)

As shown above, Sonne was extensively considered during prosecution of the ’942 and ’439 applications, and was the basis, either alone or in combination with Meezan (and at times Lehat), for every prior art-based rejection applied by the Examiner during the eight-year prosecution history of this patent family. Thus, factors (a) and (c) favor exercising our discretion to deny the Petition under § 325(d).

2. Factor (b)

Factor (b) looks to the cumulative nature of the asserted art and the prior art evaluated during examination. Because the Sonne and Meezan references were actually addressed during prosecution, we need not address whether they are cumulative to the art that the Examiner considered. *See NHK Spring Co. v. Intri-Plex Techs., Inc.*, IPR2018-00752, slip. op. at 13 (Paper 8) (PTAB Sept. 12, 2018) (precedential).

3. Factor (d)

Factor (d) looks to the extent of overlap between the arguments made during examination and the manner in which Petitioner relies on the prior art or Patent Owner distinguishes the prior art.

a. Petitioner’s Arguments with Respect to Sonne and Meezan

Petitioner’s obviousness analysis starts with Example 11 of Sonne, reproduced below, which is a “solution of diazepam” that can be used as a nose drop.

Example 11

A solution of diazepam, eg. as nosedrop, (25 g):

Diazepam	1.250 g
α-Tocopherol	10.000 g
Triacetin	13.750 g

A less concentrated formulation of diazepam is needed for the rectal administration, but still it can be very difficult to find an acceptable vehicle with low irritation.

Ex. 1013, 11:1–12. The solution of Example 11 contains diazepam, α-tocopherol, and triacetin. *Id.*; Pet. 26. Petitioner refers to this solution as DS-11. Pet. 26 n.4.

Petitioner contends that because the nosedrop of DS-11 "may be too viscous to spray," one of ordinary skill in the art would have followed Sonne's teachings and reduced the viscosity of the solution by replacing the triacetin co-solvent with ethanol. *Id.* at 27 (citing Ex. 1013, 3:60–67). Petitioner acknowledges that ethanol is "less desired" as a solvent in Sonne due to its irritation potential, but contends this does not mean that ethanol is "undesirable" or that ethanol could not be used in the nosedrop of Example 11. *Id.* at 27 n.5 (citing Ex. 1013, 1:55–63), 28 n.6 (noting that Sonne also identifies triacetin as a nose irritant). Petitioner identifies this modified "ethanol-for-triacetin replacement" containing 5% diazepam, 40% α-tocopherol, and 55% ethanol, as DS11-A. *Id.* at 28.

In view of Sonne's disclosure that co-solvents may be used to optimize the bioadhesion, sprayability, and viscosity of formulations, Petitioner contends that one of ordinary skill in the art seeking to optimize the viscosity of DS11-A would have experimented with replacing a portion of the ethanol in this solution with benzyl alcohol, thereby forming a

solution containing 5% diazepam, 40% α-tocopherol, and a combined amount of 55% ethanol and benzyl alcohol. Pet. 29–30 (citing Ex. 1013, 6:47–53). Petitioner identifies this solution as DS11-B. *Id.* at 29–30.

Petitioner contends the precise amounts of ethanol and benzyl alcohol in DS11-B would not be critical, as Patent Owner has never demonstrated criticality or unexpected results based on the relative amount of ethanol and benzyl alcohol in the solution. *Id.* at 30–31. Thus, Petitioner contends one of ordinary skill in the art would have sought to "develop DS11-B solutions containing, e.g., 30% ethanol and 25% benzyl alcohol." *Id.* at 33. In view of Sonne's disclosure that alcohol is an irritant, however, Petitioner contends one of ordinary skill in the art would have sought to replace some of the alcohol in the solution with tocopherol, which has a very low irritation potential for mucosal tissues. *Id.* (citing Ex. 1013, 2:55–58). In particular, Petitioner contends one of ordinary skill in the art would have increased the tocopherol by 25% and reduced the alcohol to 30% to arrive a solution containing 5% diazepam, 65% α-tocopherol, and 30% alcohol. *Id.* at 34–35.

Within the scope of the 30% alcohol solutions, Petitioner contends one of ordinary skill in the art would have created solutions containing various combinations of ethanol and benzyl alcohol, including solutions containing: 10% ethanol and 20% benzyl alcohol; 15% ethanol and 15% benzyl alcohol; 20% ethanol and 10% benzyl alcohol; and 19% ethanol and 11% benzyl alcohol. *Id.* Petitioner identifies the solution containing 5% diazepam, 65% α-tocopherol, 19% ethanol, and 11% benzyl alcohol as DS11-C. *Id.* at 34–35.

Petitioner further argues that because Sonne discloses generally increasing bioavailability of its invention, one of ordinary skill in the art

would have sought "to add small amounts of dodecyl maltoside, perhaps 0.25%," as disclosed in Meezan, to achieve this goal. Pet. 37. Petitioner contends ethanol would be reduced in this solution by the same percentage as dodecyl maltoside is added, resulting in a solution containing 5% diazepam, 65% α-tocopherol, 18.75% ethanol, 11% benzyl alcohol, and 0.25% dodecyl maltoside. *Id.* Petitioner identifies this solution as DS11-D. *Id.*

Petitioner relies on hypothetical solutions DS11-A, DS11-B, DS11-C, and DS11-D in arguing that the challenged claims would have been obvious over the combined disclosures of Sonne and Meezan. *See, e.g.*, Pet. 70–71 (relying on DS11-D for disclosure of a solution containing an alkyl glycoside).

b. Analysis

Petitioner contends "the specific combination of subject matter from [the] prior art references relied upon by Petitioner did not form the basis for any of the rejections of the '876 patent." Pet. 6. Thus, Petitioner asserts it presents the Sonne and Meezan references "in a new light." [8] *Id.* at 6–7.

Although the Examiner never explicitly formulated Petitioner's hypothetical DS11-A, DS11-B, DS11-C, and DS11-D solutions, the Examiner did identify and rely on nearly every disclosure of Sonne and

[8] Petitioner also contends the Examiner's consideration of the '439 and '942 applications is not dispositive because it was directed to different claim language. Pet. 11. This is not a persuasive argument because the Examiner found that the claims of the '876 patent "are not patentably distinct from" those of the '942 application, and Petitioner does not argue otherwise. *See* Ex. 1002, 438–439.

Meezan that Petitioner relies on to formulate these solutions. *See* Prelim. Resp. 9–19 (providing a claim chart comparing the arguments made during prosecution with those made in the Petition). For example, in rejecting claims in the '942 application, the Examiner relied on Sonne's disclosures that: (1) the formulations may be in the form of solutions; (2) the disclosed solutions may be used as a nasal spray; (3) the solutions may contain diazepam and tocopherol; (4) the amount of active ingredient may be from 0.001% to 40% and the amount of tocopherol may be from 20 to 99.9%; (5) the bioadhesion, sprayability, and viscosity of the solutions may be modified through the addition of co-solvents; (6) ethanol and benzyl alcohol may be used as co-solvents; and (7) the total amount of co-solvents may be as high as 50-60%, as shown in Examples 11 and 16. Ex. 1004, 2125–2126. The Examiner also noted Meezan's disclosure of using an alkyl glycoside to improve bioavailability of an active ingredient. *Id.* at 2126–2127. These are the same general disclosures that are relied upon by Petitioner and Dr. Peppas to formulate DS11-A, DS11-B, DS11-C, and DS11-D with ethanol, benzyl alcohol, and an alkyl glycoside (DS11-D). *Compare, e.g.*, Pet 27–30 (citing Ex. 1013, 3:60–67, 6:47–53, 11:1–9 (Example 11)) *with* Ex. 1004, 2125–2126 (citing Ex. 1013, 6:47–53, 11:1–13 (Example 11)) *and* Ex. 1007, 515 (quoting Ex. 1013, 3:54–61, 3:65–66, 6:47–53).

In view of Petitioner's and the Examiner's reliance on the same general disclosures of Sonne and Meezan, we find that factor (d) also favors denying institution under § 325(d).

4. Factor (e)

Factor (e) asks whether Petitioner has pointed out sufficiently how the Examiner erred in its evaluation of the prior art. Petitioner contends the

Examiner erred in his consideration of the prior art because he failed to consider the full scope of Sonne's teachings, caused, in part, by the Applicants' incorrect characterization of the content and scope of Sonne's disclosures during prosecution. Pet. 7 (asserting that the Applicants' incorrect statements during prosecution ultimately led "the Examiner away from a full and fair consideration of Sonne").

First, Petitioner contends the Applicants incorrectly argued that Sonne's discussion of using ethanol as a viscosity-reducing agent was only in the context of introducing the purported benefits of the colloidal formulations. *Id*. According to Petitioner, this was incorrect, as the discussion of using ethanol as a solvent in Sonne was not an introduction to the benefits of emulsions, but a specific teaching that ethanol may be used to reduce the viscosity of solutions. *Id.* at 7–8 (citing Ex. 1004, 2149; Ex. 1013, 3:60–4:2).

The arguments identified by Petitioner were made in an April 1, 2014 Response. *Id.* at 7 (citing Ex. 1004, 2149). Both before and after these assertions were made, the Examiner broadly applied Sonne's teachings of reducing viscosity through the addition of co-solvents. For example, in an October 1, 2013 Office Action, the Examiner stated that Sonne discloses that ethanol may be used to optimize the viscosity of the formulations. Ex. 1004, 2125. Likewise, in a July 14, 2016 Office Action in the '439 application, the Examiner stated that Sonne teaches "[v]iscosity can be reduced by the addition of co-solvents such as ethanol" and that "[a] co-solvent such as ethanol can be used in order to optimize the formulations bioadhesion, sprayability, and viscosity." Ex. 1007, 3096–3097 (citing Ex. 1013, 3:65–66, 6:47–53). Thus, even if the Applicants' arguments regarding Sonne's

ethanol disclosures were incorrect, we are not persuaded that these arguments tainted the Examiner's analysis of Sonne or caused the Examiner to narrow his broad understanding of Sonne's disclosures.

Second, Petitioner contends Example 11 is "clearly a solution" intended for use as a "nosedrop," yet the Applicants referred to Example 11 of Sonne as being directed to oil-in-water emulsions with a high concentration of oil. Pet. 9–10 (citing Ex. 1007, 501–502, 564, 2833). We agree with Petitioner that Applicants' were clearly incorrect in repeatedly characterizing the composition of Example 11 as an emulsion. Ex. 1013, 11:1–12 (identifying the composition of Example 11 as "[a] solution of diazepam . . . ."). But there is no evidence that the Applicants' faulty analysis of Sonne ever affected the Examiner's broad interpretation of Sonne's disclosures. Indeed, both before and after these misstatements were made (and subsequently abandoned (*compare* Ex. 1007, 501 *with id.* at 3085)), the Examiner continued to rely upon Example 11 of Sonne in rejecting claims within the patent family. *See* Ex. 1004, 2125 (relying on the disclosures of Sonne's Example 11); Ex. 1007, 477 (relying on Example 11 of Sonne in the first substantive Office Action of March 18, 2011), 3070, 3096, 3314, 3473 (relying on Example 11 of Sonne to reject pending claims in an October 19, 2017 Office Action).

Finally, Petitioner contends the Examiner mistakenly believed that Sonne does not disclose alkyl glycosides. Pet. 10 (citing Ex. 1013, 4:50–53, 6:54–59 (disclosing the use of "cetearyl glucoside"), 10:61, 13:17). It is not evident, however, why any possible misunderstanding regarding the use of alkyl glycosides in Sonne is relevant to the Examiner's ultimate conclusion, as both the Examiner and the Petition rely on Meezan for the disclosure of

using specific amounts of alkyl glycosides to improve bioavailability of active ingredients. *See* Ex. 1004, 2126; Pet. 36–39 (asserting that one of ordinary skill in the art would have been motivated to add 0.25% dodecyl maltoside (an alkyl glycoside) to the solutions of Sonne in view of Meezan).

In view of the foregoing, we are not persuaded that the Examiner failed to consider the full scope of Sonne's teachings or that any misstatements made by the Applicants during prosecution of the '439 and '942 applications materially affected the Examiner's broad understanding of Sonne's disclosures. Thus, factor (e) is, at best, neutral.

5. Factor (f)

Factor (f) asks whether Petitioner provides additional evidence and facts in the Petition that warrant reconsideration of the prior art or arguments.

Petitioner contends it provides additional evidence in the form of the declaration testimony of Dr. Peppas that was not before the Examiner. Pet. 7, 11. We agree that the Examiner did not have the benefit of Dr. Peppas's declaration when he allowed the challenged claims. The Examiner did, however, consider the same disclosures of Sonne that are relied upon by Dr. Peppas in his declaration, and the evidence of record does not suggest that the Examiner misunderstood these disclosures or their breadth. Thus, we are not persuaded that the presence of Dr. Peppas's declaration is sufficient to warrant reconsideration of the same prior art that was before the Examiner during prosecution. Accordingly, this factor is, at best, neutral with respect to exercising discretion under § 325(d).

6. Consideration of the Becton Dickinson Factors as a Whole

When considered in combination, *Becton Dickinson* factors (a), (c), and (d) strongly favor exercising our discretion to deny the Petition under 35 U.S.C. § 325(d). It is simply not an efficient use of the Board's time and resources to revisit the same prior art disclosures that were examined in detail by the Examiner over eight years of patent prosecution. The fact that Petitioner and Dr. Peppas formulate new hypothetical compounds based on Example 11 of Sonne, which was identified and relied upon by the Examiner during prosecution, does not warrant the Board retreading the same worn path the Examiner and the Applicants travelled during the extensive prosecution history in this patent family. Accordingly, we determine that the *Becton Dickinson* factors, when considered as a whole, support exercising our discretion to deny the Petition under 35 U.S.C. § 325(d).

III. CONCLUSION

For the reasons set forth above, we exercise our discretion under 35 U.S.C. § 325(d) and do not institute *inter partes* review of the challenged claims.

IV. ORDER

It is

ORDERED that the Petition is *denied* and no *inter partes* review is instituted.

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